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Title: EPIDEMIOLOGICAL FORECASTING FOR REAL-TIME OUTBREAK MANAGEMENT

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5 JUN 2003

Los Alamos
NATIONAL LABORATORY

EPIDEMIOLOGICAL FORECASTING FOR REAL-TIME OUTBREAK MANAGEMENT

(LA-UR- 03-3980)

Norman L. Johnson
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Los Alamos National Laboratory

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Abstract

Objectives:

The goal is to provide decision makers with a tool for the real-time forecasting of consequences of alternative management strategies in the event of an outbreak of an infectious agent. The scope of the capability will include cities, regions, nations or the world. The accuracy of forecasts will be enhanced by the assimilation of incoming data during the course of an epidemic, in an analogous manner to the use of current meteorological data in weather prediction. Forecasts will initially focus on the state of health of individuals during the epidemic (e.g., ill, dead, recovered), but will later extend to community-level economic and behavioral (e.g., panic, trauma) consequences. The project builds on our experience with the development of EpiSims (CBNP funded in FY00-02 under PI C. Macken).

Salient features of the software architecture will include:

• Ability to assimilate, in real time, data from medical, environmental and population surveillance systems to continually refine and improve epidemiological forecasts.
• Modularity to facilitate adaptation to different surveillance resolutions and qualities, different classes of pathogens, and different geographical locations and demographics.
• Fast, nimble software designed using state-of-the-art computer science techniques, to enable rapid response on a variety of platforms.

The project also includes the creation of a unique national resource: an individually-resolved data set collected during the course of a real influenza epidemic, specifically developed for the validation and verification of individually-resolved epidemiological simulations.

Recent Progress:

The project started in January, 2003. As illustrated in Fig. 1, the four core technical activities (in blue) are being pursued in parallel, coordinated by the planning for the overall architecture of EpiCast.

To speed the development of the capability, an existing modular system that addresses the above goal was selected and is currently being tested; this system was developed for simulating and visualizing molecular dynamics , arguably a near relative to agent-based simulations. We have demonstrated the flexibility of this capability by reproducing the results of a recent study of a bioterrorist event involving smallpox. The

original work generated statistics from 50 realizations of simulated outbreaks in communities of 2000 people each. We have demonstrated that we can simultaneously examine 505,600 realizations of simulations involving 2000 people each - or over one billion people total - on Los Alamos' open QSC machine. (Using 128 processors, it took 7 hours of wall-clock time to simulate an epidemic over a course of 365 days.) From this baseline study, we are using a model of interconnected communities to expand our simulations to cities and to large regions. On this same platform, we are beginning to research methods for assimilation of real-time data, a complex theoretical problem.
To select the level of description required in the model, we are using EpiSims to evaluate the sensitivity of predictions to various choices about the model of an epidemic. We have been able to identify important and unimportant variables; these insights are guiding our design of EpiCast. For example, for an influenza outbreak in Portland, OR, runs of EpiSims show that the global characteristics of the epidemic (e.g., number of new infections) are insensitive to large changes in the population mobility when the epidemic is randomly seeded throughout the population. Yet, we observe that the course of the epidemic is sensitive to specific seeding into different groups of family size or ages. When possible, we are comparing our predictions with an analysis that we carried out earlier this year of the data from the "Seattle Flu Watch", in which respiratory infections in several hundred households were tracked over time between 1975 and 1979.
To make progress on the adaptive population mobility model, which includes changing behavior patterns as a consequence of the epidemic, we have engaged an industrial collaborator, Innovative Emergency Management (IEM). IEM has expertise in modeling public responses to a crisis. They will provide user requirements for the development of EpiCast from their sponsors. We have also developed a general model for individual behavior that combines a variety of validated behavior models (habitual, social, rational, differential).
The two remaining components, the individual immune model and the inter-person transmission model, are of sufficient readiness to await development in the other components.

Future Outlook:
By the end of FY03, we will have a scalable EpiCast tool (without data assimilation) as a demonstration capability that is executable on platforms ranging from a PC to a supercomputer. In FY04, we will begin the planning and execution of the validation data set, with Prof. Samet of The Johns Hopkins University and Dr. Wiese, Institute of Public Health, UNM. The data assimilation methodology will be developed and implemented in FY04, with a baseline capability in early FY05. While developed for epidemics, this methodology has broad applicability across all homeland security activities that involve rich data streams and comparable simulations. The EpiCast capability can also be used within training tools, for example those currently under development by Sandia National Laboratories for public health officials.

This work was carried out under the auspices of the National Nuclear Security Administration of the U.S. Department of Energy at Los Alamos National Laboratory under Contract No. W-7405-ENG-36

Biological Countermeasures

Epidemiological Forecasting (*EpiCast*) for Real-time Outbreak Management

Presentation for the

CBNP 2003 Summer Meeting

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LANL – Catherine Macken, Kai Kadau, Tim Germann, Krastan Blagoev, Peter Lomdahl, Tim McPherson
Innovative Emergency Management, Inc. – Dr. Mike Boechler
Univ. of New Mexico – Prof. Robert Balance
John Hopkins University – Prof. Jonathon Samet
New Mexico State Department of Health - Dr. Bill Wiese
SNL and LLNL

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Ideas That Change the World

1

Opportunity for an Epidemiological Defense Capability

Traditional epidemiology is a historical study to prevent future epidemics

Epidemiology is currently undergoing a revolution, comparable to the past changes in weather quantification and prediction

Similar driving factors are present in both cases:

- ✓ Vastly increased and higher quality data sources
- ✓ Improved understanding of the basic processes
- ✓ Advanced computing/information resources

Existing national resources which can be coordinated and integrated:

- ✓ Active environmental and syndromic biosurveillance programs
- ✓ Forefront computational immunology research
- ✓ Individual-resolved epidemiological modeling (*EpiSims*)
- ✓ Critical infrastructure simulation and analysis (*NISAC*)
- ✓ World-class computing resources

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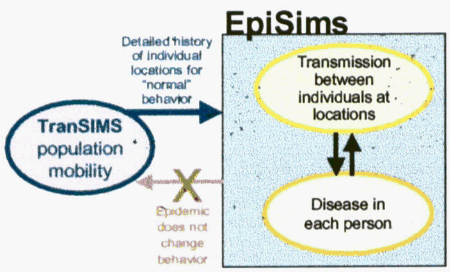
EpiSims

Funded by CBNP in FY00-02 and by NISAC
Combines unique national laboratory capabilities:

- ✓ TranSIMS: individually-resolved population mobility simulation
- ✓ Computational individual immune model



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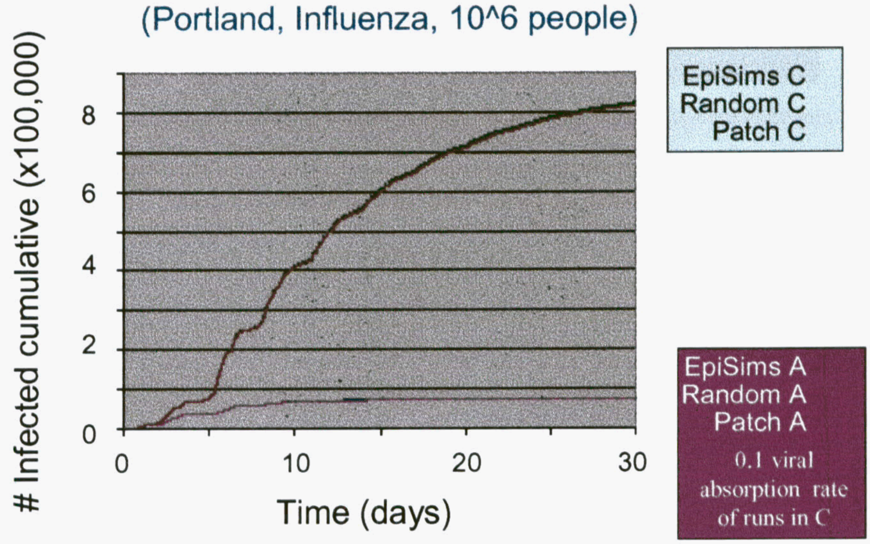
Transportation Sensitivity with EpiSims
(Portland, Influenza, 10^6 people)



Conclusions: complete insensitivity of mobility under some conditions, Sensitivity to immune response of individuals

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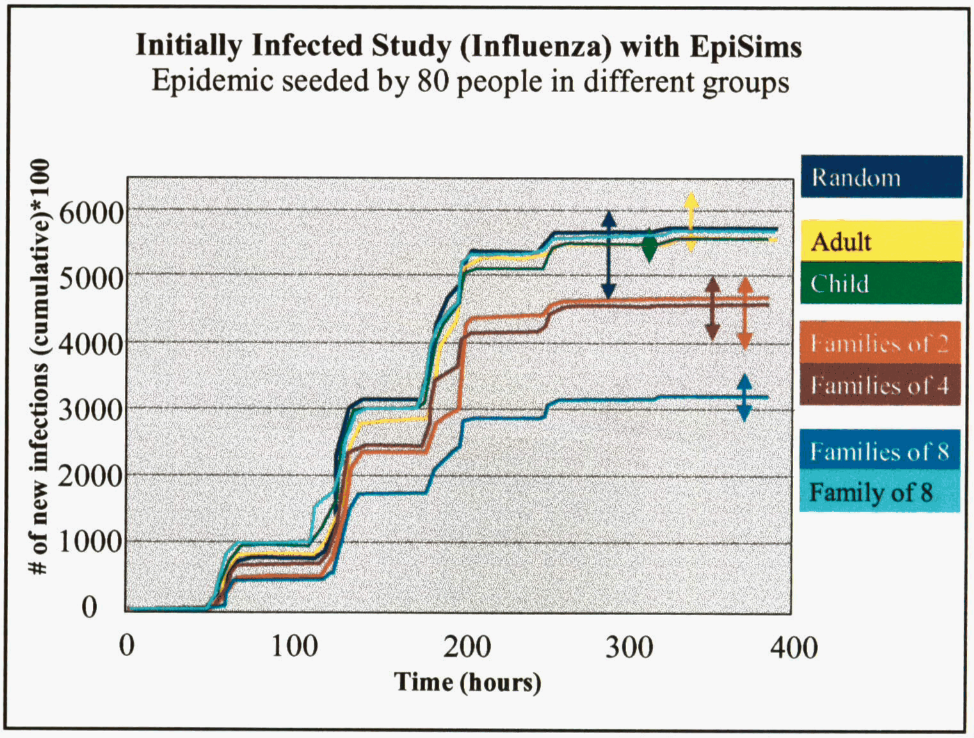

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Real-world Influenza Data

"Family Flu Study" conducted 1975-79 in Seattle

Household infection:

Household size		% Uninfected	% Infected
	2	85	15
	3	66	34
	4	41	59
	5	34	66
	6	21	79
Pearson correlation coefficient		*-0.988*	*0.981*

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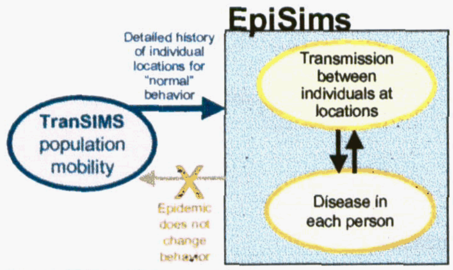
EpiSims



Major Conclusions:

- ✓ Sensitivity to individual mobility is dependent on initial seeding
- ✓ Individual immune modeling is almost always important
- ✓ Modifications in behavior (e.g., self-quarantine) is required

Broader sampling of realizations and validation is essential at this time

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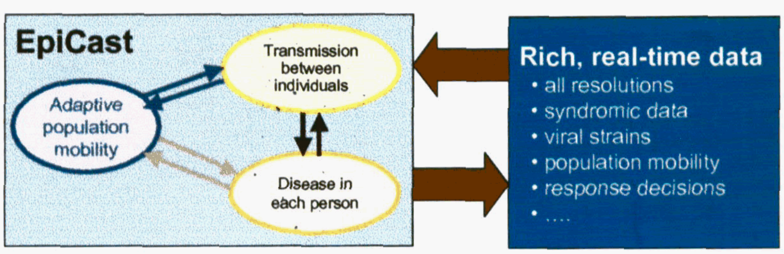
Transition from EpiSims to EpiCast

EpiCast makes two fundamental additions to EpiSims:

- The ability of the individuals to adapt their behavior to an epidemic
- The ability to "assimilate" data to improve the accuracy of the prediction of the epidemic

Use EpiSims to guide simplification without reducing accuracy



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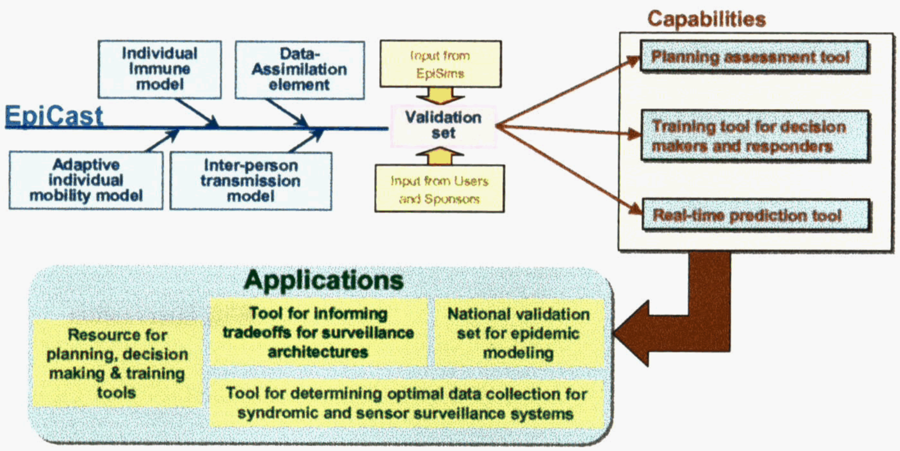
EpiCast Project Roadmap Summary

EpiCast - an integrated library of modules for the simulation of the evolution of an epidemic, typically resolved at (but not restricted to) the individual level.

Goals

- Provide faster than real-time assessment of mitigation strategies during an epidemic
- Capture health, economic, and psychological consequences of an epidemic



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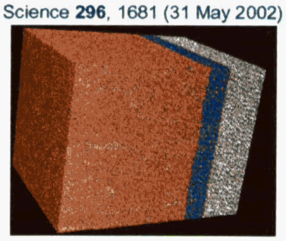
Applying the NW expertise in multimillion-atom simulations to agent-based models

Microscopic View of Structural Phase Transitions Induced by Shock Waves

Kai Kadau,[1,2*] Timothy C. Germann,[2] Peter S. Lomdahl,[1] Brad Lee Holian[1]

Multimillion-atom molecular-dynamics simulations are used to investigate the shock-induced phase transformation of solid iron. Above a critical shock strength, many small close-packed grains nucleate in the shock-compressed body-centered cubic crystal growing on a picosecond time scale to form larger, energetically favored grains. A split two-wave shock structure is observed immediately above this threshold, with an elastic precursor ahead of the lagging transformation wave. For even higher shock strengths, a single, overdriven wave is obtained. The dynamics and orientation of the developing close-packed grains depend on the shock strength and especially on the crystallographic shock direction. Orientational relations between the unshocked and shocked regions are similar to those found for the temperature-driven martensitic transformation in iron and its alloys.

Science **296**, 1681 (31 May 2002)



Containing Bioterrorist Smallpox

M. Elizabeth Halloran,* Ira M. Longini Jr., Azhar Nizam, Yang Yang

The need for a planned response to a deliberate introduction of smallpox has recently become urgent. We constructed a stochastic simulator of the spread of smallpox in structured communities to compare the effectiveness of mass vaccination versus targeted vaccination of close contacts of cases. Mass vaccination before smallpox introduction or immediately after the first cases was more effective than targeted vaccination in preventing and containing epidemics if there was no prior herd immunity (that is, no prior immunologic protection within the population). The effectiveness of postrelease targeted and mass vaccinations increased if we assumed that there was residual immunity in adults vaccinated before 1972, but the effectiveness of targeted vaccination increased more than that of mass vaccination. Under all scenarios, targeted vaccination prevented more cases per dose of vaccine than did mass vaccination. Although further research with larger-scale structured models is needed, our results suggest that increasing herd immunity, perhaps with a combination of preemptive voluntary vaccination and vaccination of first responders, could enhance the effectiveness of postattack intervention. It could also help targeted vaccination be more competitive with mass vaccination at both preventing and containing a deliberate introduction of smallpox.

Science **298**, 1428 (15 Nov 2002)

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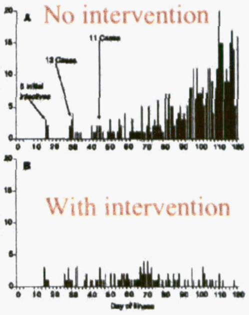
The Longini Community Model for Smallpox

- 4 neighborhoods plus common schools (daycare, elementary, etc)
  Transmission in families > schools > neighborhoods > community
- Households have 1 to 7 people
- 5 age groups (2 child, 3 adult)
- Stochastic spread within multiple contact groups
- Age-dependent transmission probabilities
- Time-varying infectiousness (viral production rate)
- **Behavioral modification of symptomatic individuals**

Fig. 1. Natural history of smallpox infection in our model. The duration of each of the three main periods is uniformly distributed between its minimum and maximum periods. During the prodromal period, the probability of people's staying home by the third day of symptoms is similar to the probability given by the influenza model in (21). All people stay home within 3 days of developing pox.

Incubation	Prodromal	Pox
• 10-14 days • 12 day mean • 100% of infected people ill by end of day 14 • sensitive to vaccine during first 3 days after infection	• 3-5 days • 4 day mean • highly infectious • probability of withdrawal by day 3: preschool 0.8 school: 0.75 adult 0.50	• 14-17 days • 15.5 day mean • infectiousness: 10% of prodromal phase • withdrawal over first 3 days (100% by 3rd day) • recovered/removed after completing this phase

Fig. 2. The first 120 days of typical stochastically simulated smallpox epidemics with five initial infective persons in communities with no prior residual immunity in people who are 30 years of age and older. (A) Baseline with no intervention. (B) Intervention with targeted vaccination, with 100% ascertainment begun after the first indigenous secondary case. The simulated epidemics without intervention last on average ~300 days.



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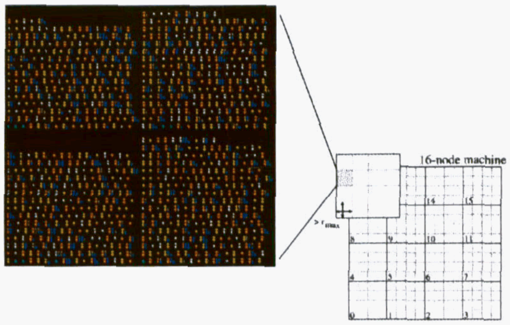
Billion-person simulations of smallpox epidemics

- ✓ Each 2000-person community is mapped to a computational cell
- ✓ Initially non-interacting communities (travel is readily added)
- ✓ Trial simulations on QSC (128 processors, 7 hours wall-clock): 505,600 communities (1.01×10^9 people)



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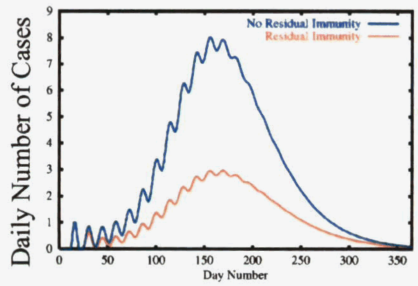
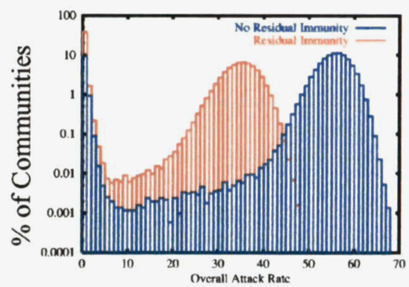
What is the effect of residual immunity (no recent vaccination)?

- ✓ Two cases: pre-1972 vaccinations have 0% or 50% efficacy
- ✓ Bimodal attack rate distributions:
  Either an initial outbreak is avoided, or a major epidemic develops with attack rates ~35% and 56%, with and without prior residual immunity, respectively
- ✓ With the enormous sampling, possible outliers can be found in << 0.1% of the communities - better risk prediction of outliers





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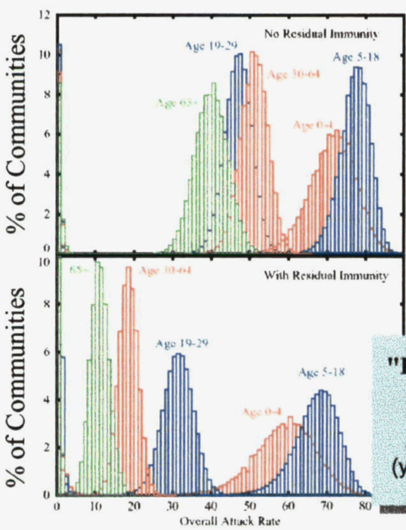
Results by age



- ✓ Schools and daycare transmission is important
- ✓ Adult protection due to residual immunity has a minor benefit to children
- ✓ Elderly people are protected by their relative isolation

"Family Flu Study" conducted 1975-79 in Seattle

Age (years)	Exposed	Infected	Attack Rate
0-18	55%	80%	45.0%
>18	45%	20%	13.5%

p < 0.001

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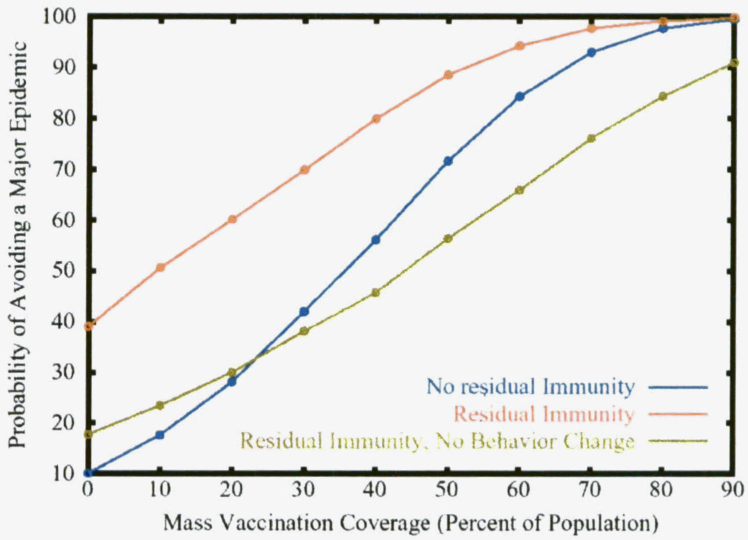
Effect of Vaccination



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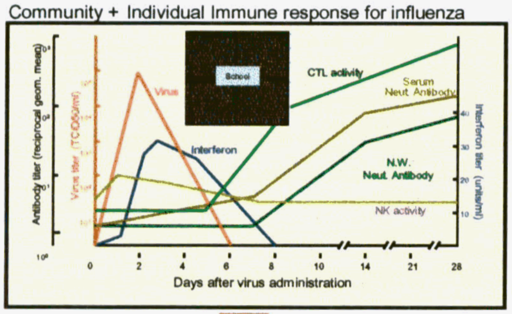
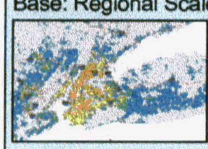
Future of a Capability of Modeling a Million Communities

Community + Individual Immune response for influenza



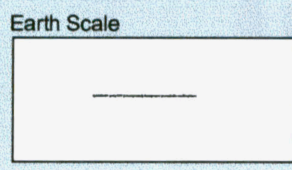
Larger systems are communities connected by long-range transportation

Base: Regional Scale



National Scale

Earth Scale



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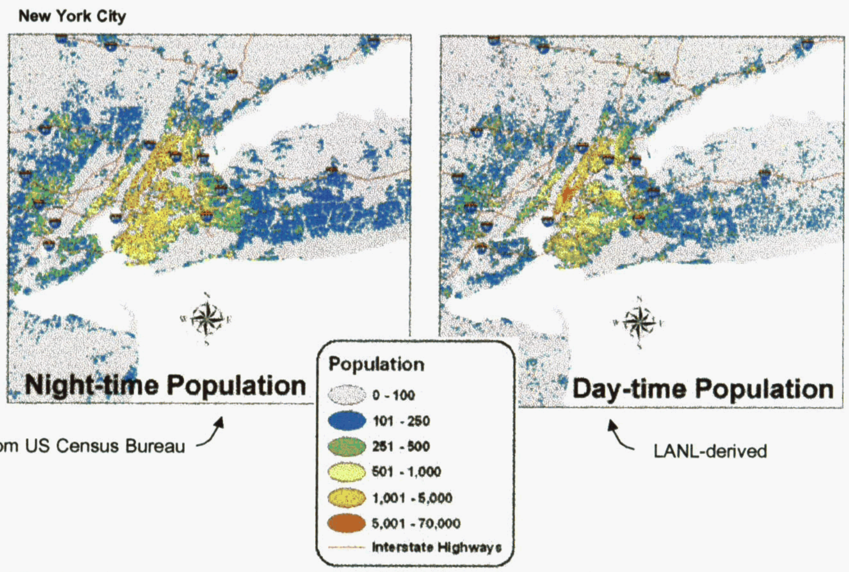
Day vs. Night Population

Creation of daytime population database for over 100 US Cities



From US Census Bureau

LANL-derived

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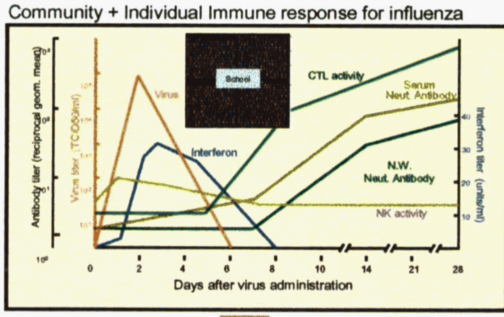
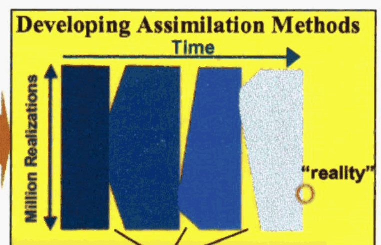
Future of a Capability of Modeling a Million Communities

Community + Individual Immune response for influenza

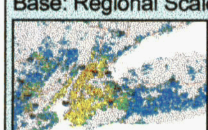




"data feeds" eliminate unrealistic paths +
Realization space is repopulated =
Know more about less

Larger systems are communities connected by long-range transportation

Base: Regional Scale



National Scale

Earth Scale

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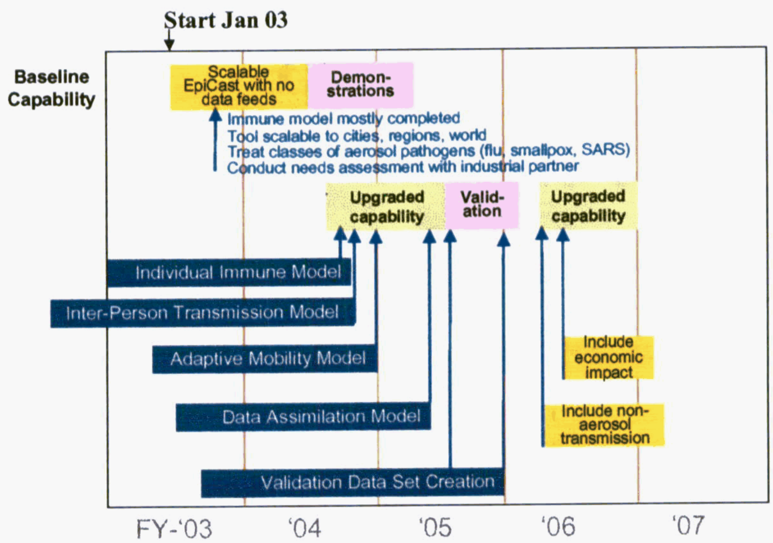
Lifecycle Roadmap for EpiCast Project



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Treat symptoms? Detect to treat? Detect to warn?

Current focus of the DHS program is Urban monitoring

- ✓What type of laboratory tests are needed? How quickly? How accurate?
- ✓What sensors are needed? How accurate? How fast? How cheap?
- ✓What decision support system is needed? How robust? How responsive?
- ✓What synergy is possible with the daily health-care systems?

Threat Origin (internal, external, natural)

Prepara-tion	Threat	Medium	Disper-sion	Amplifica-tion	Detection	Mitiga-tion	Re-sponse
None	Anthrax	Food	None	None	None	None	None
Vaccination	Smallpox	Air	Wind	Low infectiousness	Syndromic	Vaccine	Deaths
Environmental surveillance	Ebola	Water	Mail system	Moderate infectiousness	Exterior samples	Medication	Health care
Syndromic surveillance	Influenza	Envelopes	Social contact	High infectiousness	Interior samples	Quarantine	Societal (panic,…)
Drug caching, Training, …	Unknown: SARS, …	People, infrastructure, …	HVAC, vectors …	Morbidity, incapacitation, symptoms, …	Sensor networks, …	Evacuation …	Economic, decon, …

Consequences: high – low

20

An example - 2001 Amerithrax

Threat Origin (internal, external, natural)

Prepara-tion	Threat	Medium	Disper-sion	Amplifica-tion	Detection	Mitiga-tion	Re-sponse
None	Anthrax	Food	None	None	None	None	None
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Syndromic surveillance	Influenza	Envelopes	Social contact	High infectiousness	Interior samples	Quarantine	Societal (panic,...) X
Drug caching, Training	SARS, …	People, infrastructure, …	HVAC, vectors …	Morbidity, incapacitation, symptoms, …	Sensor networks, …	Evacuation …	Economic decon, …

high
Consequences
low

21

Another example - SARS

The "biggest" effect was change of social behavior and the consequent economic impact.

Threat Origin (internal, external, natural)

Prepara-tion	Threat	Medium	Disper-sion	Amplifica-tion	Detection	Mitiga-tion	Re-sponse
None	Anthrax	Food	None	None	None	None	None
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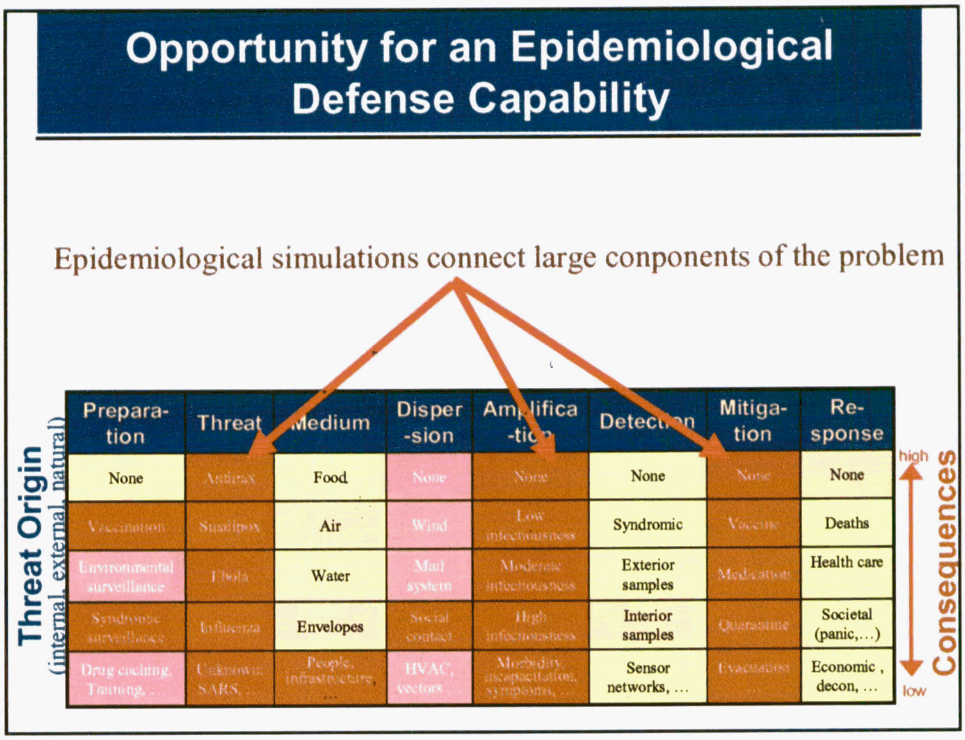
Drug caching, Training, …	Unknown SARS…	People, infrastructure	HVAC, vectors …	Morbidity, incapacitation, symptoms, …	Sensor networks, …	Evacuation …	Economic decon, …

high
Consequences
low

22


Opportunity for an Epidemiological Defense Capability
Epidemiological simulations connect large conponents of the problem
Prepara-tion
Threat
Medium
Disper-sion
Amplifica-tion
Detection
Mitiga-tion
Re-sponse
None
Anthrax
Food
None
None
None
None
None
Vaccination
Smallpox
Air
Wind
Low infectiousness
Syndromic
Vaccine
Deaths
Environmental surveillance
Ebola
Water
Mail system
Moderate infectiousness
Exterior samples
Medication
Health care
Syndromic surveillance
Influenza
Envelopes
Social contact
High infectiousness
Interior samples
Quarantine
Societal (panic,…)
Drug caching, Training, …
Unknown: SARS, …
People, infrastructure …
HVAC, vectors …
Morbidity, incapacitation, symptoms, …
Sensor networks, …
Evacuation
Economic, decon, …
Threat Origin
(internal, external, natural)
Consequences
high
low

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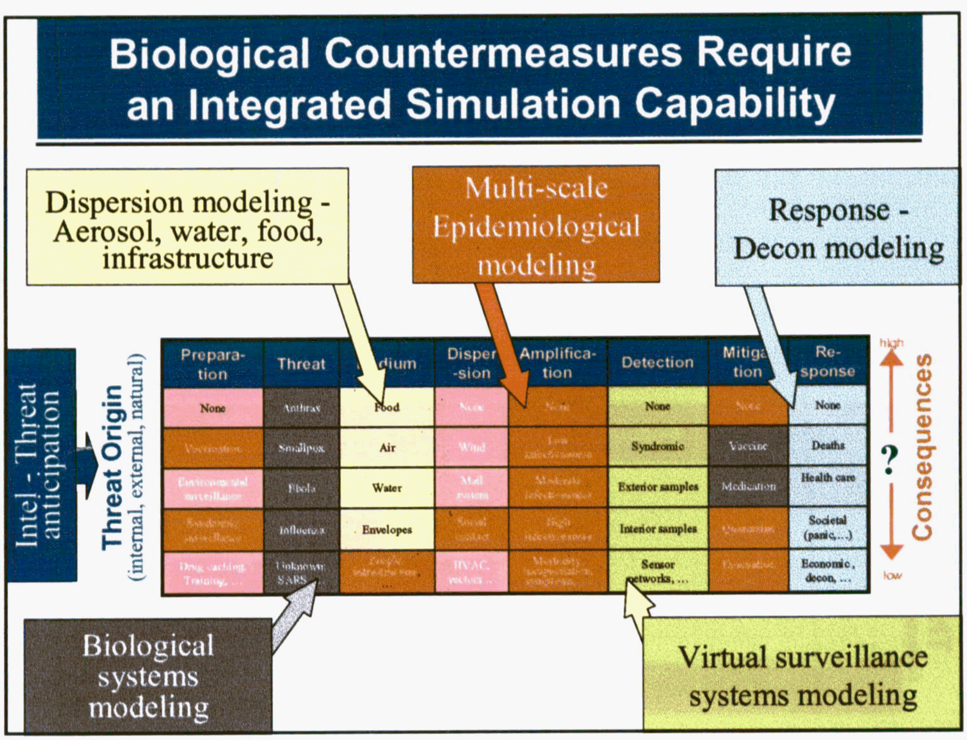
Biological Countermeasures Require an Integrated Simulation Capability
Dispersion modeling - Aerosol, water, food, infrastructure
Multi-scale Epidemiological modeling
Response - Decon modeling
Intel - Threat anticipation
Threat Origin
(internal, external, natural)
Prepara-tion
Threat
Disper-sion
Amplifica-tion
Detection
Re-sponse
None
Anthrax
Food
None
Vaccination
Smallpox
Air
Syndromic
Vaccine
Deaths
Ebola
Water
Exterior samples
Medication
Health care
Influenza
Envelopes
Interior samples
Societal (panic,…)
Unknown: SARS
Sensor networks, …
Economic, decon, …
Consequences
?
high
low
Biological systems modeling
Virtual surveillance systems modeling

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